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Research Article

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Physical impact and health-related quality of life of SCD in adults: the Real-World Portuguese ASCEND Study

Christopher J. Saunders, MD[1,2], Madalena Martins, MD[1], Marinela Major, MD[3], Catarina Favas, MD[3], Ana Tomé, MD[4], Fernanda Vargas, MD[4], Joana Rosa Martins, MD[5,6,7], Ryan Silva Costa, MD[5,6,7], Maria Manuel Deveza, MD[7,8], Filipa Pires, MD[8], Tabita Magalhães Maia, MD[9], João Gaião Santos, MD[9], Celeste Bento, MD[9,10], Inês Fonseca, MD[11], Inês Moital, PhD[12], Daniel Brás, PharmD[12,13,*]

[1]Unidade Local de Saúde de São José—Hospital Santo António dos Capuchos, Lisboa 1150-199, Portugal
[2]Católica Medical School, Universidade Católica Portuguesa, Lisboa 2635-631, Portugal
[3]Unidade Local de Saúde de Amadora/Sintra—Hospital Professor Doutor Fernando da Fonseca, Amadora 2720-276, Portugal
[4]Unidade Local de Saúde de Almada/Seixal—Hospital Garcia de Orta, Almada 2805-267, Portugal
[5]Unidade Local de Saúde de Santa Maria—Hospital Santa Maria, Serviço de Medicina Interna, Lisboa 1649-028, Portugal
[6]Clínica Universitária de Medicina I, Serviço Hospitalar de Medicina I, Unidade Local de Saúde de Santa Maria, Lisboa 1649-028, Portugal
[7]Faculdade de Medicina da Universidade de Lisboa, Lisboa 1649-028, Portugal
[8]Unidade Local de Saúde de Santa Maria—Hospital Santa Maria, Serviço de Imunohemoterapia, Lisboa 1649-028, Portugal
[9]Unidade Local de Saúde de Coimbra—Hospitais da Universidade de Coimbra, Coimbra 3000-075, Portugal
[10]APPDH—Associação Portuguesa de Pais e Doentes com Hemoglobinopatias, Almada 2810-274, Portugal
[11]Hospital de Cascais Dr. José de Almeida, Cascais 2755-009, Portugal
[12]Novartis, Produtos Farmacêuticos SA, Porto Salvo 2740-255, Portugal
[13]NOVA National School of Public Health, Public Health, Comprehensive Health Research Centre, CHRC, Universidade NOVA de Lisboa, Lisboa 1600-407, Portugal

*Corresponding author: Daniel Brás, PharmD, Avenida Professor Doutor Cavaco Silva 10- 10E6, Taguspark, Lisbon 2740-255, Portugal (daniel.bras@novartis.com).

Abstract

Objectives: **SCD negatively impacts patient's health-related quality of life (HRQoL). The ASCEND study investigated how SCD impacts the HRQoL of adults in Portugal, focusing on its physical, emotional, and social burdens.**

Methods: **This non-interventional, cross-sectional study included two cohorts of adult SCD patients from seven Portuguese Reference Centers (Cohort 1) and the Portuguese Patient Association (Cohort 2). Sociodemographic and patient-reported outcomes were collected for both cohorts, along with clinical data for Cohort 1, between February and September/2022.**

Results: **211 adult SCD patients (Cohort 1: 200; Cohort 2: 11) were included (median age of 33.0 years, 58.8% male). Nearly 90% reported complications. Patients were diagnosed at a median age of 2.0 years, mainly with the HbSS variant (89.0%), and 86.0% were under treatment (73.5% on hydroxyurea, 45.0% on chronic transfusion). All had lifetime pain episodes, with 72.6% experiencing at least one in the previous year. Most (91.9%) adopted daily strategies to prevent pain episodes, 67.1% had pain management plans, and 46.7% self-managed crises at home. Pain/discomfort (60.6%) and anxiety/depression (51.0%) were major problems (median EQ-5D-5L score = 0.91), affecting emotional well-being (53.8%) and/or social life (49.0%). Indeed,**

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less frequent pain significantly correlated with improved HRQoL (*P* = .001). While 40.0% felt neglected, 70.5% rarely or never experienced solitude, and 84.6% reported a sense of support.

Conclusion: **The ASCEND study reveals the multifaceted impact of SCD on adults in Portugal and its influence on HRQoL, emphasizing the need for a multidisciplinary care approach and effective self-management education to improve patient outcomes.**

Keywords SCD, health-related quality of life, pain episodes, self-management, multidisciplinary care

Lay summary

The ASCEND study aimed to understand how SCD, a blood disorder known to cause severe pain episodes, affects the lives of adults in Portugal. A total of 211 patients participated in the study, self-reporting how they experienced and managed disease symptoms and how these affected their day-to-day life. The results showed that pain episodes were not only common but also had a substantial impact on various aspects of patients' lives, causing physical, emotional, and social distress. Despite having the support and knowledge necessary to prevent and manage these episodes, patients still perceived a negative impact of SCD on their lives, which was significantly linked with the frequency of these episodes. By providing valuable insights into the reality of the adult population with SCD in Portugal, this study emphasizes the importance of comprehensive care and patient education to improve self-management strategies for individuals living with SCD in order to maximize their quality of life.

Introduction

In 2021, the number of newborns with SCD surpassed the half-million mark, with around 8 million people living with the disease worldwide[1]—mainly in Africa and India. In the same year, the prevalence of the disease in Portugal was estimated by disease experts at 800–900 cases.[2] Nevertheless, these are not official data for the country, which are still lacking and of utmost importance.

Individuals with SCD experience a spectrum of complications, including chronic hemolysis, anemia, and vaso-occlusion.[3,4] Vaso-occlusive crises (VOC), marked by intense acute pain, emerge as a hallmark of SCD and typically first manifest in infants around the age of 5 months. These acute episodes are painful, debilitating, and unpredictable, requiring analgesic therapy. They are the leading cause of hospital admissions and healthcare resources use in adults with SCD,[5,6] even though patients can manage these crises at home with specific coping strategies. Unfortunately, the current treatment options for SCD are limited. New treatment options based on gene therapy have been approved as of the end of 2023 by the Food and Drug Administration, Casgevy[7] and Lyfgenia,[8] offering a new hope for curing these patients and improving their health-related quality of life (HRQoL). Notwithstanding this recent milestone, patients still require a multidisciplinary care to manage pain, and the complications associated with the disease. However, accessing quality healthcare and adequate treatment is frequently a challenge, particularly when transitioning from pediatric to adult care.[9,10]

SCD, particularly pain episodes, has a major negative impact on patients' HRQoL.[10-13] It is often accompanied by psychological, cognitive, and emotional issues that severely affect personal relationships, work productivity, education, social life, and daily activities. Still, the impact of SCD and its management on HRQoL is poorly documented and understood, necessitating a comprehensive definition of health that encompasses physical, mental, and social well-being. In Portugal, recent studies have shed light on the clinical and sociodemographic characteristics of children and adolescents with SCD, as well as the acute complications they experience, highlighting the substantial impact of the disease on their HRQoL.[14-16] However, this knowledge remains untapped in Portuguese adult patients.

By thoroughly analyzing the intersections between clinical manifestations, treatment modalities, and patient-reported outcomes (PROs), the ASCEND (Assessing physical, SoCial and EmotioNal impact of sickle cell Disease in Portuguese patients) study aims to bridge this knowledge gap regarding the impact of SCD on adult patients' lives and associated challenges. The inclusion of patients from both hospital settings and those recruited by a national patient advisory group provides a broader characterization of the SCD burden in a real-life setting. The ultimate goal is to provide valuable insights for targeted interventions that go beyond symptom management, by identifying unmet needs and addressing barriers to care.

Materials and methods

Study design and study sample

ASCEND was a non-interventional, cross-sectional, real-world study of adult patients diagnosed with SCD. It included 7 Portuguese reference hospitals for SCD, located in central and southern Portugal, where the prevalence of the disease is highest (*Unidade Local de Saúde de São José – Hospital Santo António dos Capuchos*, *Unidade Local de Saúde de Amadora/Sintra—Hospital Fernando da Fonseca*, *Unidade Local de Saúde* *de Almada/Seixal—Hospital Garcia de Orta*, *Unidade Local de Saúde de Santa Maria—Hospital de Santa Maria*—Internal Medicine and Immunohemotherapy Services, *Unidade Local de Saúde de Coimbra*, and *Hospital de Cascais*), as well as the Portuguese Patient Association (APPDH, *Associação Portuguesa de Pais e Doentes com Hemoglobinopatias*).

This study included two cohorts of patients with a confirmed SCD diagnosis: cohort 1 included individuals who attended a clinical appointment at one of the participating centers during the study period; and cohort 2 comprised individuals recruited by the APPDH.

Patients were considered eligible for study participation if they had signed the informed consent and met all the following inclusion criteria: patients with confirmed SCD diagnosis, regardless of genotype, with 18 years of age or older. Subjects who had a sickle cell trait diagnosis, or a non-confirmed diagnosis of SCD were excluded from the study.

Data collection and outcome measures

Primary and secondary data were collected between February and September 2022. Primary data included sociodemographics [age, gender, Body Mass Index (BMI), occupational status, and nationality], questionnaires assessing disease follow-up, VOC management, healthcare resource use, and both social and emotional burden of disease, and the PROs ASCQ-Me and EQ-5D-5L. The ASCQ-Me evaluated the frequency and severity of VOC crises in the past 12 months[17]; the EQ-5D-5L examined the impact of the disease on the patient's HRQoL by assessing mobility, self-care, usual activities, pain/discomfort, and anxiety/depression in individuals with SCD.[18] Secondary data comprised clinical information (age at diagnosis, disease genotype, complications, most recent laboratory test results, current treatment for SCD [HU, chronic blood transfusions, iron chelation therapy], and concomitant medications).

Primary data were collected directly from digital questionnaires for both cohorts, while secondary data were collected exclusively for cohort 1.

Statistical analysis

Numerical variables were described by measures of central tendency (median) and dispersion (P25, P75: 25th and 75th percentiles, respectively). Categorical variables were summarized as absolute (n) and relative (%) frequencies. Percentages were calculated based on non-missing values.

Continuous variables were compared between three or more independent subgroups using the Kruskal-Wallis test and between two independent subgroups using the Mann-Whitney *U* test. The correlation between two numerical variables, whether discrete or continuous, with a non-normal distribution was evaluated using the non-parametric Spearman's correlation coefficient.

P-values were corrected for multiple comparisons using the Benjamini-Hochberg method with a false discovery rate of .05. All the statistical analyses were performed using RStudio software version 4.2.2. Graphical representations were generated using RStudio 4.2.2 and Excel software.

Results

Patients' sociodemographic and clinical characteristics

The flow diagram of the study sample is depicted in Figure 1.

The sociodemographic characteristics of the study sample are outlined in Table 1. In summary, the median [P25; P75] age was 33.0 [25.0; 42.0] years, and patients were predominantly male (58.8%) with a normal weight (67.6%; BMI = 18.5–24.9 kg/m^2). Most had achieved secondary education (71.1%) and had a professional occupation—either employed (48.8%) or students (21.3%). Most participants were Portuguese (56.4%), followed by Angolans (21.8%), and Sao Tomeans (6.6%).

The clinical characterization of patients was restricted to the 200 individuals from cohort 1 (Table 2 and Table S1). Patients were diagnosed at a median age of 2.0 [0.0; 5.0] years, approximately 27 years before entering the study. Of these, 18 (9.0%) patients were diagnosed only during adulthood. The HbSS variant of the disease was the most prevalent (89.0%). The majority of patients had history in their medical records of at least one complications (89.5%), with splenic sequestration (26.0%), hepatobiliary disorders (26.0%), and acute chest syndrome (19.5%) being the most frequent. The incidence of patients with acute SCD-related complications (47.0%) was higher than that of patients with chronic complications (27.5%), with splenic sequestration (26.0%) and ulcer (13.0%) being the most common acute and chronic complications, respectively. In addition, 17.0% of patients presented both acute and chronic complications, while 42.5% had neither. Table 2 also details the most recent laboratory test results from these patients.

SCD and pain episodes' management

After being diagnosed with SCD, patients were cared for mainly by hematologists (67.6%) or physicians of different

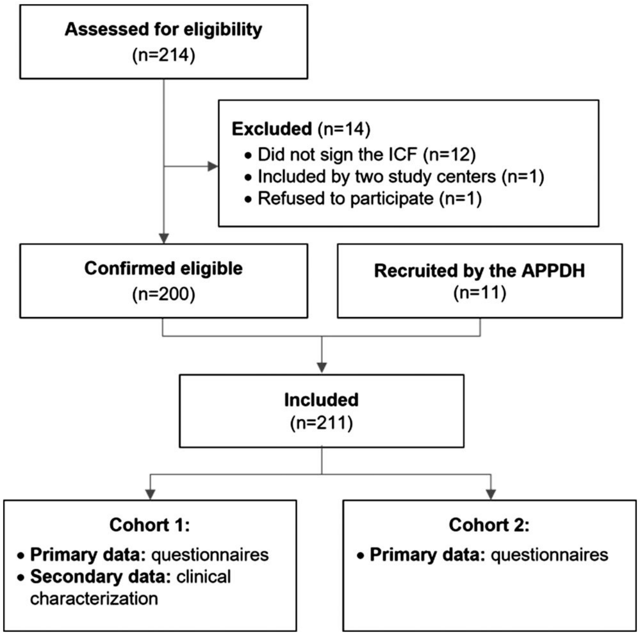

Figure 1 Flow diagram of the study sample.

Table 1 Sociodemographic characteristics of the study sample.

Sociodemographic characteristics	n **= 211**
Age (years)	
Median [P25; P75]	33.0 [25.0; 42.0]
Minimum/Maximum	18/67
Male, *n* (%)	124 (58.8)
BMI (kg/m^2), *n* (%)	
<18.5	32 (15.2)
18.5–24.9	142 (67.3)
25.0–29.9	31 (14.7)
≥30.0	6 (2.8)
Median [P25; P75]	21.9 [19.5; 23.9]
Educational level, *n* (%)	
None	2 (0.9)
Elementary education	43 (20.4)
Secondary education	107 (50.7)
Higher education	59 (28.0)
Occupational status, *n* (%)	
Employed	102 (48.3)
Student	45 (21.3)
Unemployed	34 (16.1)
No professional occupation	19 (9.0)
Retired	11 (5.2)
Nationality, *n* (%)	
Portuguese	119 (57.5)
Angolan	46 (22.2)
Sao Tomean	14 (6.8)
Other	28 (13.5)
Missing	4 (1.9)

Abbreviation: BMI: body mass index.

Table 2 Clinical characteristics of the study sample.

Clinical characteristics	n **= 200**
Genotype, *n* (%)	
HbSS	178 (89.0)
HbSC	15 (7.5)
HbSβ+ thalassemia	3 (1.5)
HbSβ0 thalassemia	4 (2.0)
Age at diagnosis (years), median [P25; P75]	2.0 [0.0; 5.0]
Disease duration (years), median [P25; P75]	27.0 [20.0; 36.0]
Complications, *n* (%)	
At least one	179 (89.5)
Acute[a]	94 (47.0)
Chronic[b]	55 (27.5)
Acute and chronic	34 (17.0)
Other conditions	85 (42.5)
Laboratory values, median [P25; P75]	
Hb (g/dL)	8.7 [7.8; 9.9]
HbF (%)	7.4 [2.7; 12.1]
Haematocrit (%)	25.0 [22.1; 28.3]
Neutrophils ($\times 10^9$/L)	4.6 [3.2; 5.8]
Platelets ($\times 10^9$/L)	330.0 [241.0; 419.0]
Creatinine (mg/dL)	0.6 [0.5; 0.8]
eGFR (mL/min/1.73 m2)	126.0 [109.0; 153.0]
Bilirubin (mg/dL)	2.1 [1.3; 3.1]
ALT (U/L)	20 [14; 28.8]
	n **= 200**
Treatment for SCD, *n* (%)	
Yes	172 (86.0)
HU	147 (73.5)[c]
Blood transfusions (chronic)	90 (45.0)[c]
Exchange transfusion	37 (41.6)[d]
Iron chelation therapy	27 (13.5)[c]
Other	2 (1.0)[d]

[a] At least one of the following: splenic sequestration, acute chest syndrome, stroke, priapism, and myocardial infarction.

[b] At least one of the following: ulcer, chronic pulmonary disease, moderate or severe kidney disease, congestive heart failure, chronic, moderate or severe hepatic disease, and peripheral vascular disease.

[c] Relative frequency calculated within the 200 patients of cohort 1.

[d] Relative frequency calculated within the 90 patients with blood transfusions.

ALT: alanine transaminase; eGFR: estimated glomerular filtration rate; Hb: hemoglobin; HbF: fetal hemoglobin; HbSC: hemoglobin SC disease; HbSS: hemoglobin SS disease; HU: hydroxyurea; SCD: sickle-cell disease.

clinical specialties (Table S2). Among those diagnosed in childhood, nearly half (45.6%) faced various difficulties in the transition from pediatric to adulthood care: lack of a healthcare professional with expertise in the disease (55.9%), lack of transfer of their medical records (35.5%), or increased waiting time for a new medical appointment (29.0%).

Almost 90% of the patients were receiving treatment for the disease (Tables S2 and S3). HU (hydroxyurea) was the most common (73.5%), either alone (39.5%) or in combination (46.3%) with blood transfusion, iron chelation and/or other SCD treatment. Blood transfusions were given to 90 patients (45.0%), including 37 (41.6%) who received exchange transfusion, and iron chelation to 27 (13.5%), while only 1% of SCD patients received any other type of treatment. In addition, 97.0% of individuals received at least one concomitant medication, the majority of which were antianemics (90.5%). Smaller proportions were prescribed antihypertensives (25.1%), non-steroidal anti-inflammatory drugs (24.5%), anticoagulants/antithrombotics (19.5%), opioid analgesics (11.0%), and vitamin supplements (9.5%).

During the COVID-19 pandemic, the study allowed for an assessment of its impact on patients' disease management. In general, most patients (65.2%) perceived that the pandemic had minimal or no effect on how they handle their disease (data not shown).

Frequency, severity, and management of pain episodes

In line with the primary outcome, the physical impact of SCD was evaluated through the ASCQ-Me questionnaire. It assessed the frequency and severity of pain episodes in the past year in the 201 individuals who completed this PRO (Figure 2). While all patients had experienced at least one pain episode in their lifetime, 72.6% had suffered at least one in the previous 12 months. Within this timeframe, 15.9% reported having only one episode, 11.4% had two, 14.9%

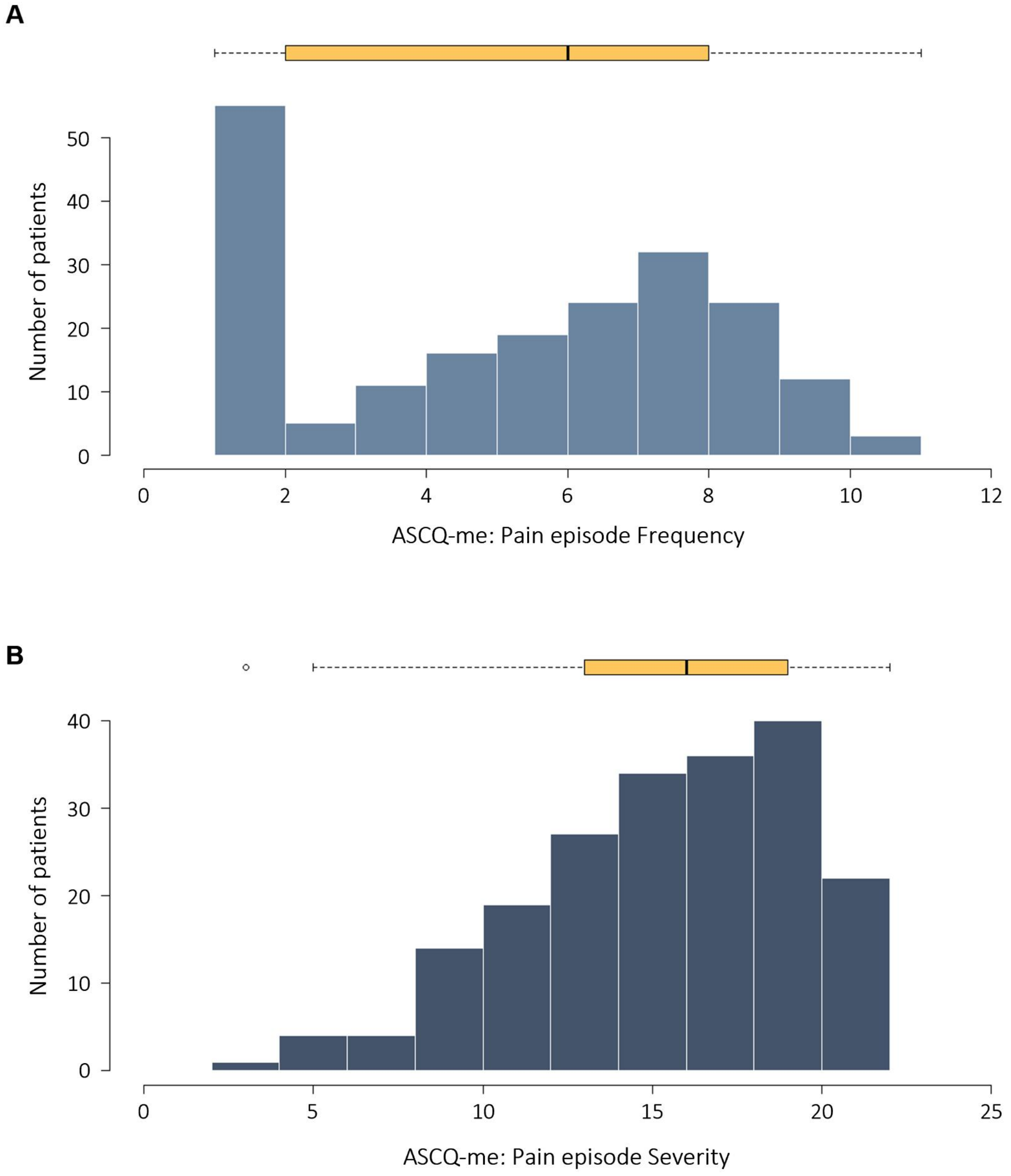

Figure 2 ASCQ-Me scores distribution. Pain episode (A) frequency and (B) severity score distribution histograms in SCD patients in the last 12 months. Frequency values range from 0 to 11 and severity values from 0 to 22. The histogram shows the distribution of pain frequency and severity scores. The boxplot represents the median (middle line) and the first and third quartiles (box ends). The extreme right of the boxplot error bar shows the maximum and the extreme left circle shows the minimum.

had three, and 30.3% had four or more pain crisis. When assessing the severity of the most recent episode, the median score was 9.0 [6.0, 10.0], in a scale where 0 represents "no pain" and 10 refers to the "worst pain imaginable." Overall, the median ASCQ-Me score for the frequency of pain episodes during the last year was 6.0 [2.0; 8.0] on a 0 to 11 scale (Figure 2A), and the median ASCQ-Me score for their severity was 16.0 [13.0, 19.0] on a 0 to 22 scale (Figure 2B), respectively. Additionally, ASCQ-Me median frequency score was significantly ($P = .006$) higher for patients undergoing exchange transfusion than for the patients without transfusion treatment (Table S4). The number of VOCs increased with decreasing BMI ($\rho = -0.142$, $P = .045$) and the frequency of pain episodes was higher in patients prescribed HU, compared to those who were not ($P = .038$), with similar severity scores ($P = .094$). Moreover, neither the frequency ($\rho = -0.110$, $P = .120$) nor severity ($\rho = -0.052$, $P = .467$) correlated with patient age (data not shown).

Most SCD patients (91.9%) adopted daily strategies to proactively prevent pain episodes, such as staying hydrated (89.6%), avoiding sudden temperature changes (65.8%), maintaining a proper diet (55.4%), having a regular sleep schedule (30.1%), and limiting working hours (11.9%) (Table S2). Additionally, over half of the patients (67.1%) had a pain management plan provided by their medical team. Still, during a crisis, 39.0% required regular, and 52.4% needed occasional assistance. Nearly 47% self-managed their crisis at home, while 43.3% sought help at the hospital

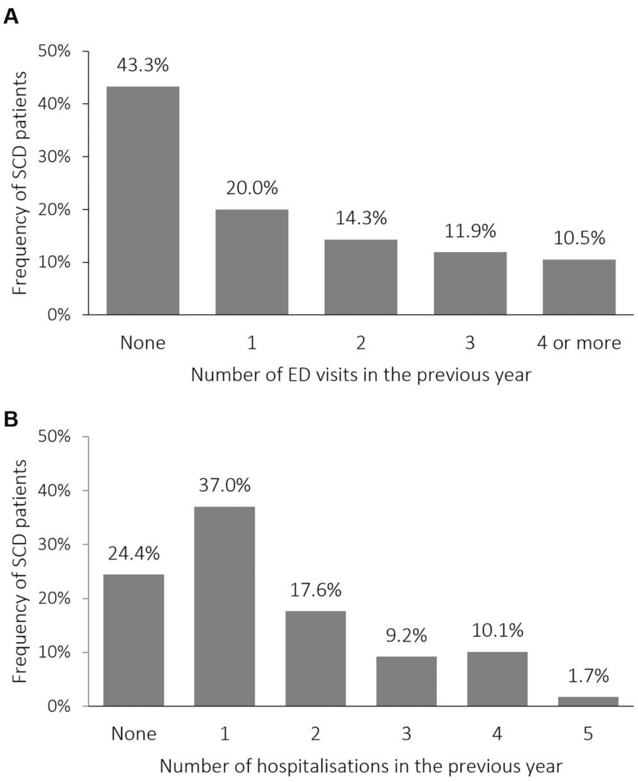

Figure 3 Emergency department (ED) visits and hospitalization of SCD patients due to pain episodes in the previous year. Frequency of patients who visited the emergency department (A) and were hospitalized (B) to solve a pain episode. Relative frequencies were calculated within the 210 patients who answered the disease and VOC management questionnaire and within the 119 patients visited ED to solve a VOC crisis (A and B, respectively).

emergency department. Only 6.7% and 3.3% of the individuals resolved their pain episodes through specific consultations at the hospital or within the health community (pharmacy, primary care), respectively.

Regarding pain crisis, 56.7% of SCD patients visited the emergency department (ED) at least once in the previous year (Figure 3A), and 75.6% were hospitalized up to five times in the same period (Figure 3B).

Patient's health-related quality of life

The impact of the disease and associated pain episodes on patient's HRQoL was assessed across several dimensions, through the EQ-5D-5L questionnaire (Figure 4). In general, patients reported more problems with pain/discomfort (60.6%) and anxiety/depression (51.0%), of whom 2.4% and 1.0% of patients had extreme pain/discomfort and felt extremely anxious/depressed, respectively. The least problematic dimensions were self-care (13.5%), mobility (35.1%), and usual activities (39.4%), with over 60% of patients reporting no problems in these areas (Figure 4A) Still, between 1.0% and 1.4% of patients were unable to care for themselves, walk, or carry out usual activities. The median EQ-5D-5L index score was 0.91 [0.79, 0.96], ranging 0 to 1, being 1 the best health possible. Moreover, the median patients' self-rated overall health status on the day of the EQ-5D-5L questionnaire, represented by the VAS score, was 77.0 [59.3; 90.0], in a graduated scale from 0 to 100, with higher scores meaning better HRQoL (Figure 4B).

Younger patients had better EQ-5D-5L index values ($P = .005$, Figure S1), which decreased as age increased ($\rho = -0.221$, $P = .001$). Also, higher VAS scores ($P = .007$), indicating an improved HRQoL, were associated with a lower number of hospitalizations due to VOCs (data not shown). EQ-5D-5L index scores did not differ significantly between exchange transfusion, normal transfusion or patients without transfusion (Table S4).

A negative burden of SCD on different aspects of patient's lives was frequent (Table 3). About half of the patients perceived a negative emotional impact (53.8%) and/or interference with their social life (49.0%). To a lesser extent, economic status (35.1%), relationships with others (14.9%) and family (13.5%) were also affected. Importantly, while a significant proportion of patients (40.4%) felt neglected because of SCD, most felt supported (84.6%) and rarely or never felt alone (70.5%) when coping with this disease.

Correlation between pain episodes and the patient's HR-QoL

The correlation between the ASCQ-Me and the EQ-5D-5L scores evaluated the impact of VOC pain frequency and severity on the patients HRQoL (Table 4). As expected, a lower frequency of pain episodes was significantly correlated with improved QoL ($P = .001$). Contrarily, the correlation between pain severity and EQ-5D-5L VAS and index scores did not follow the same tendency ($P = .536$; $P = .719$, respectively).

Discussion

The ASCEND study provides the first real-world characterization of the impact of SCD on the HRQoL of adult patients in Portugal. These findings reveal that SCD has a significant physical, social, and emotional impact on patients, with a high prevalence of pain episodes and a wide range of acute and chronic complications. These findings underscore the necessity for a comprehensive multidisciplinary approach to SCD patient management, offering healthcare providers valuable insights that can improve patient care beyond symptom's management.

This sample consisted mainly of young (median age 33 years), healthy weight, Portuguese adult men, presenting predominantly the HbSS subtype.[19] While the higher prevalence of SCD in men contrasts with other samples, the higher frequency of the HbSS disease subtype is consistent, although considerably higher in the current study.[10,12,20,21] Most patients had completed secondary education and were either employed or students. Socioeconomic status not only predicts whether SCD complications affect a patient's employment[22] but also influences access to healthcare. A literature review has shown that low socioeconomic status hinders access to healthcare, with income being the most influential factor.[23]

Nearly all patients had history of at least one complication and about half reported acute ones, namely splenic

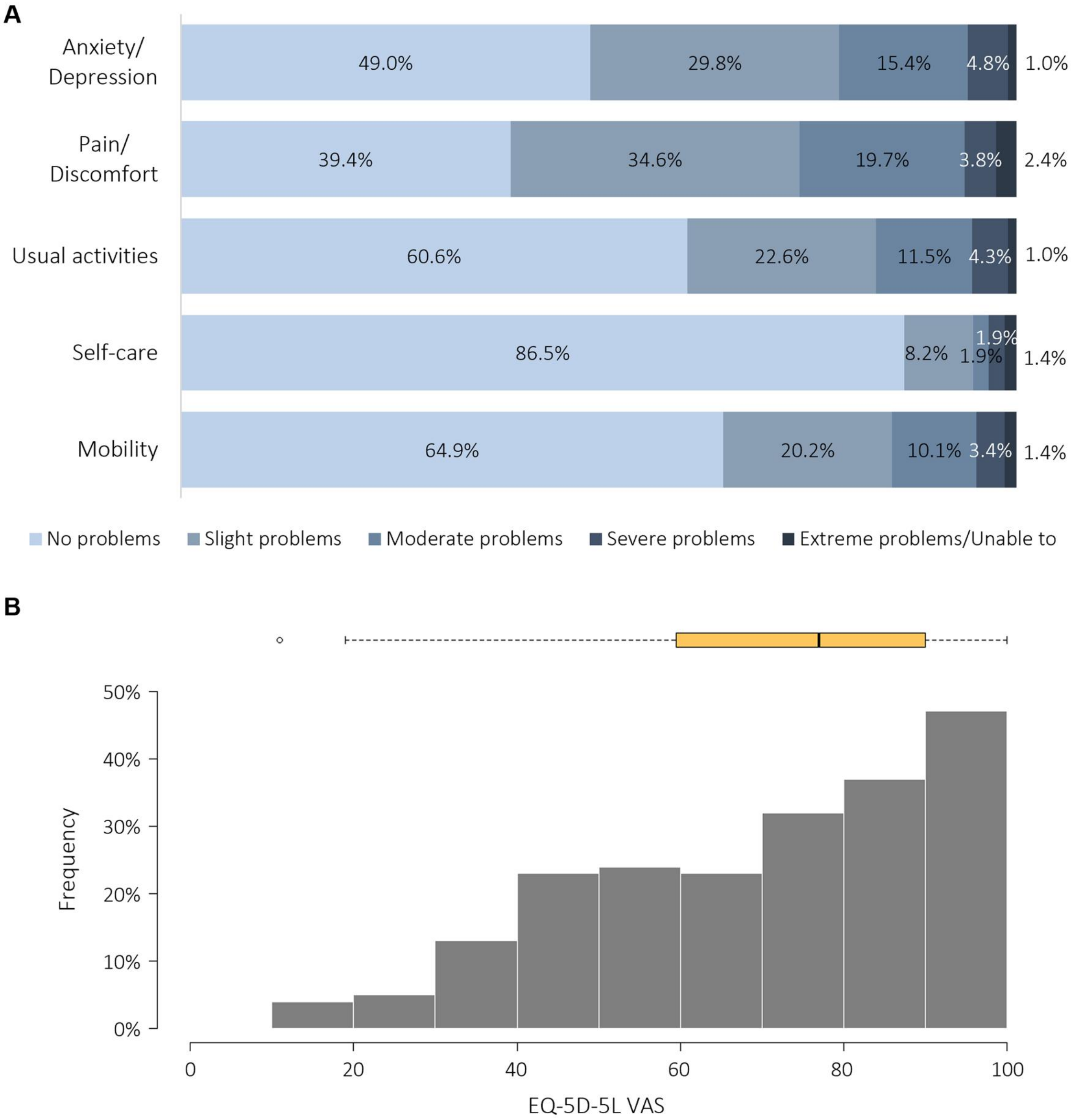

Figure 4. HR-QoL of patients with SCD. (A) EQ-5D-5L scores by level and dimension. Data are shown as the relative frequency of patients within each dimension. (B) Histogram showing the distribution of SCD patients' self-rated overall health status on the day of EQ-5D-5L questionnaire. EQ-5D-5L VAS score ranged from 0 to 100.

sequestration and acute chest syndrome, which require a multidisciplinary approach for patient management.[11,24] This approach includes guidance on treatment, education about SCD, and access to psychological, social, and health support. The proportion of patients with a history of ACS in our cohort is lower than typically reported in SCD populations.[25] Our data relied on documented ACS episodes in clinical records, and under-reporting or incomplete historical information which may have led to an underestimation of lifetime ACS prevalence. Moreover, a substantial proportion of patients were enrolled in chronic transfusion programs, which may have contributed to preventing ACS episodes. The presence of complications or symptoms associated with the disease impacts patients' daily activities and ability to work, ultimately affecting their HRQoL.[26] Additionally, patients reported median pain episodes ASCQ-Me scores of 6.0 and 16.0 for frequency and severity, respectively, with the majority (72.6%) having experienced one or more pain episodes in the previous year. These results emphasize the substantial burden of pain associated with the disease. Comparable ASCQ-Me scores were reported in a USA cohort, where 91.1% of patients had experienced at least one VOC in the year prior to study inclusion.[10]

The use of healthcare resources due to pain episodes was significant, as expected.[5,6,10] During the year before enrollment, about 60% of patients visited the ED at least once and about half were hospitalized. Still, nearly half of individuals managed their pain episodes at home and the majority adopted daily strategies for VOC prevention, demonstrating the effective education and preparation of patients in self-managing painful crises at home, often resulting from their consistent follow-up by specialized healthcare professionals.

Table 3 Impact of SCD on different areas of patient's lives.

	n **= 211**
Main aspects negatively affected by SCD,[a] *n* (%)	
Emotional	112 (53.8)
Social	102 (49.0)
Economical	73 (35.1)
Relationship	31 (14.9)
Family	28 (13.5)
Other	8 (3.9)
Don't know/Don't answer	8 (3.8)
Missing	3 (1.4)
Feeling of having been neglected due to SCD, *n* (%)	84 (40.4)
Feeling supported in dealing with the disease, *n* (%)	176 (84.6)
Feeling of loneliness, *n* (%)	
Every day	17 (8.2)
Every week	14 (6.7)
Every month	22 (10.6)
Rarely	87 (42.0)
Never	59 (28.5)
Don't known/Don't answer	8 (3.9)
Missing	4 (1.9)

Abbreviations: SCD: sickle cell disease.

[a] Multiple response option.

Table 4 Correlation between the ASCQ-Me and the EQ-5D-5L VAS and index scores.

Parameters		**Correlation coefficient**[a]	***P*-value**
ASCQ-Me	**EQ-5D-5L**		
Pain episode frequency vs	VAS	−0.335	.001
	Index	−0.310	.001
Pain episode severity vs	VAS	−0.044	.536
	Index	−0.026	.719

Abbreviations: ASCQ-Me: adult sickle cell quality of life measurement system; VAS: visual analogue scale.

[a] Spearman's correlation considering pain frequency and severity scores as continuous variables. *P*-value < .05 was considered statistically significant.

Understanding and identifying self-management activities for pain prevention and management prior to care-seeking is of paramount importance not only for patient wellbeing but also to alleviate the burden and cost to the healthcare system.[27,28] To support this claim is the fact that most patients felt that the COVID-19 pandemic, which limited the access to ED and hospitals, had little or no impact on the management of their disease. Nevertheless, it remains unclear whether the pandemic may have resulted in reduced exposure to risk factors for pain episodes and therefore lower VOCs, or whether the Sars-CoV2 infection plays a protective role or acts as a trigger for SCD complications.[29]

A number of factors negatively impact the HRQoL, such as work productivity, education, and social life of children and adults with SCD.[10-13,16,30] For instance, McClish *et al.* showed that the health of US adults with SCD was physically and mentally severely compromised, with an worse HRQoL than patients with other chronic diseases[12]; Rizio *et al.* also demonstrated that patients with more frequent and severe VOCs had worse HRQoL and work productivity.[10] Complications such as asthma and avascular necrosis were also shown to decrease SF-36 health status scale scores.[31] A 2024 study conducted in France has shown that use of painkillers, financial situation and support from relatives are predictors of HRQoL in SCD.[32] Patients with chronic complications, female patients, and patients with psychological follow-up had worse physical functioning score. In contrast, a better mental function score was associated with stable financial situation and presence of relative's support. The present study supports these observations by showing worse HRQoL in older patients, in those with higher ASCQ-Me pain frequency scores, and with more hospitalizations. Differences in patient's management and advances in treatment options over the years, or increased compliance of younger patients to healthcare recommendations may explain such findings. Of relevance was also the considerable proportion of patients who were unemployed despite being of working age. Pain/discomfort and anxiety/depression were the psychological dimensions causing the most problems to SCD patients. In fact, most patients stated the emotional and social impact of the disease, with a concerning 25.6% of patients often feeling lonely, which also affected their relationships and ability to work. A recent Portuguese study of pediatric SCD patients and their parents revealed that children's HRQoL worsened with increasing age, pain frequency, and number of hospitalizations, particularly in the areas of psychosocial, physical, emotional, social, and school functioning.[16] Despite the negative effect of the disease, nearly all patients in this study were being followed for disease management and the majority believed they had the necessary support to cope with the disease, particularly from their family and healthcare specialist. Overall, these results support Rizio *et al.* suggestion that VOCs have cumulative effects on various aspects of life, extending beyond the duration of the events themselves.[10]

SCD stigmatization is a challenge for young adults. It can begin in childhood and become more evident in the transition from pediatric to adult care.[9] Actually, the challenges faced by young adults in this transitioning phase may be one of the contributing factors that explain the negative impact of SCD on various aspects of their lives. Accordingly, nearly half of this study's patients reported some kind of difficulty with this transition, mainly related to the lack of specialized healthcare professionals or increased waiting time for a medical appointment. These challenges may affect their ability to receive appropriate treatment and are another compelling reason to advocate for specialized and multidisciplinary consultations to support the follow-up of patients with SCD.[33]

The vast majority of patients received treatment and/or specific procedures for SCD, with the first-line therapy for SCD, HU, being the most common option, followed by blood transfusions, particularly exchange transfusions. HU has been shown to modify the disease severity and morbidity by reducing the frequency of pain episodes and of acute chest syndrome, as well as the need for blood transfusions and hospitalizations in children and adults with SCD.[4,34,35] The indications for transfusions were met according to the guidelines in force at the time.[36,37] In this study, patients who received HU experienced higher pain episode frequencies compared to those who did not receive this treatment. While the cross-sectional design of this study hinders the understanding of whether patients on HU naturally had more painful crises or patients were prescribed HU in response to more frequent crises, a retrospective study of 102 children described a decreased incidence of VOCs after HU initiation.[38] Additionally, the ASCQ-Me median frequency score was significantly higher in the exchange transfusion group compared with the no-transfusion group, despite similar median severity scores. Given the cross-sectional nature of this study and the absence of data on the clinical indications for initiating exchange transfusion, it is not possible to determine whether exchange transfusion itself contributes to higher reported pain frequency or whether this finding primarily reflects greater baseline disease severity in this subgroup. Despite HRQoL not varying in these subgroups, EQ-5D-5L may be less sensitive to changes in pain patterns or disease-specific experiences as it provides a broader assessment of general health status. In sum, this knowledge could lead to more informed treatment decisions and tailored management plans, ultimately improving the overall care and HRQoL for people with SCD.

The ASCEND is a real-world characterization of patients with SCD in Portugal, involving national reference hospitals with dedicated medical teams focused on the disease. It included a significant number of patients and involved comprehensive data collection across various dimensions, thus contributing to a better understanding of the disease in Portugal, especially of pain episodes. Still, it is not without limitations. Due to its cross-sectional nature, this study does not allow to draw causal conclusions, such as the association between the prescription of HU and the frequency of pain episodes. It also does not address key aspects of SCD such as the impact of the disease on work productivity or education. Although fatigue—a relevant and burdensome SCD symptom—was not evaluated in this study, it is known to be negatively correlated with HRQoL scores.[39] Some variables such as biological parameters (mean corpuscular volume, reticulocyte count, LDH) were not collected. Moreover, there might be a potential geographic bias of the recruited population since most of the participating centers were located in the central region of Portugal. It is also important to recognize that, although PROs are a valuable tool for understanding patients' perspectives, their subjective nature may impact the accuracy and reliability of the data. Finally, incomplete or inconsistent questionnaire responses were also observed. For a better understanding of the disease and its management in Portugal, future research with a longitudinal design, a greater representation of the country, and the inclusion of patients newly diagnosed with SCD is important.

Conclusion

This study provides a comprehensive description of the patient experience with SCD, namely the physical, social, and emotional impact of the disease in adults in Portugal. Overall, the results emphasize the need for a multidisciplinary approach to patient management, effective education and self-management strategies for patients, and specialized support during the transition from pediatric to adult care. In the absence of a therapeutic approach that can alleviate the negative effects of SCD, which is only now becoming available, regular follow-up in specialized clinical appointments could ultimately play an important role in positively impacting patients' lives.

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Author contributions

Christopher J. Saunders (Investigation, Writing—review & editing), Madalena Martins (Investigation, Writing—review & editing), Marinela Major (Investigation, Supervision, Writing—review & editing), Catarina Favas (Investigation, Writing—review & editing), Ana Tomé (Investigation, Supervision, Writing—review & editing), Fernanda Vargas (Investigation, Writing—review & editing), Joana Rosa Martins (Investigation, Supervision, Writing—review & editing), Ryan Silva Costa (Investigation, Writing—review & editing), Maria Manuel Deveza (Investigation, Supervision, Writing—review & editing), Filipa Pires (Investigation, Writing—review & editing), Tabita Magalhães Maia (Investigation, Supervision, Writing—review & editing), João Gaião Santos (Investigation, Writing—review & editing), Celeste Bento (Investigation, Writing—review & editing), Inês Fonseca (Investigation, Supervision, Writing—review & editing), Inês Moital (Conceptualization, Methodology, Supervision, Writing—review & editing), and Daniel Brás (Conceptualization, Methodology, Supervision, Writing—review & editing)

Supplementary material

Supplementary material is available at *Journal of Sickle Cell Disease* online.

Conflicts of interest

D.B. is an employee of Novartis. I.M. was employed by Novartis at the time of this work but currently is an employee of AstraZeneca Portugal. J.R.M. declares interests with Laboratórios Vitoria/Faes Farma, Mylan/Viatris, Novartis, AstraZeneca, and Bayer. R.S.C. declares interests with Bayer. The remaining authors declare no conflict of interests.

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Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was conducted in accordance with the principles stated in the Declaration of Helsinki and Good Pharmacoepidemiology Practices (GPP). Ethical approval was obtained from the administration board and independent ethics committee of each participating site. Informed consent was obtained from all study participants.

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